22

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Title: SIMPLIFIED BLADDER TRAINING AUGMENTS TOLTERODINE TREATMENT IN OVERACTIVE BLADDER PATIENTS

Aims of Study:

Studies using bladder training (BT) without other treatments have shown impressive results in decreasing urinary symptoms [1-3]. Common procedures in these studies have been frequent interactions with patients, education, motivation and positive reinforcement. Unfortunately, many clinics do not have sufficient staff or the appropriately trained staff to provide this intensive patient interaction. Therefore, it is important to determine whether a simplified bladder training regimen would be effective in the treatment of patients with overactive bladder. Since recent evidence has shown that combining behavioral and drug therapy results in added benefits for patients with urge incontinence [4], this study compared the effect of tolterodine 2 mg bid with simplified bladder training versus tolterodine 2 mg bid alone.

Methods:

This is a multicenter, randomized, single-blind, parallel study designed to be conducted in 480 overactive bladder patients (stress and mixed incontinence patients excluded from the study) with a minimum of 8 micturitions/24h and urgency +/- urge incontinence. Patients were treated with tolterodine 2 mg bid or tolterodine 2 mg bid plus bladder training (BT) for 24 weeks with visits at baseline, 2, 12, and 24 weeks. At baseline, patients randomized to BT and tolterodine received study drug and a package containing: 12 micturition diaries, instructions for how to complete the diaries, and a single page instruction detailing the goals of BT and information about the action of antimuscarinics on the bladder. Patients randomized to tolterodine alone received study drug and a package containing: instructions for how to complete a micturition diary, and a single page with information about the action of antimuscarinics on the bladder. Micturition diaries were completed by all patients for 3 days prior to each visit. Additional visits or telephone follow-up were not allowed during the study.

The primary efficacy variable in the study was micturition frequency. Secondary efficacy parameters were urge incontinence episodes, volume voided per micturition and patient perception of bladder condition. Tolerability was assessed through adverse event reports.

Results:

A total of 501 patients were enrolled and randomized of which 244 were in the tolterodine and BT group and 257 in the tolterodine group. The groups were well balanced at baseline with regards to demographics, disease history, and baseline symptoms. Mean age of patients was 61 years, 75% were female, and 15% had previously received treatment for overactive bladder.

At two weeks after initiating treatment and continuing throughout the study, patients on both treatments had significant decreases in all micturition diary and patient perception variables from baseline. Patients in the tolterodine and BT group experienced significantly greater improvement in micturition frequency and volume

voided/micturition compared to patients in the tolterodine group (see table). A total of 76% of patients in the tolterodine and BT group reported improvement in their bladder condition compared to 71% in the tolterodine group ($p > 0.05$).

% change from baseline after 24 weeks treatment (intent to treat analysis)

Parameter	Tolterodine alone	Tolterodine plus BT	P value
Micturitions/24 hours (mean)	-24%	-34%	0.0001
Volume voided/micturition (mean)	+23%	+32%	0.01
Incontinence episodes/24 hours (median)	-81%	-87%	0.9306

The two treatments were well tolerated with no differences between the groups in % of patients completing treatment, % of patients with adverse events, withdrawals due to adverse events, or types of adverse events. A total of 77% of patients competed the study. At least one adverse event was reported by 67% of patients and 15% of patients withdrew due to adverse events. The most common adverse events in each group were dry mouth (33% of patients: 21% mild, 11% moderate and 1% severe intensity) and headache (7%) of patients. All other adverse events occurred in less than 5% of patients. No safety concerns were noted.

Conclusions:

Tolterodine is an antimuscarinic agent with proven efficacy and tolerability. The results of this study show that a simplified bladder training regiment significantly augments tolterodine treatment in overactive bladder patients. These results have implications not only for quality of patient treatment but also for medical costs.

References

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Supported by Pharmacia Corporation